A Case Study of the t(3;8)(p14.2;q24.1) Translocation: Implications for Renal Cell Carcinoma & Reproductive Challenges

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Abstract: In constitutional cytogenetics, balanced chromosomes rearrangements are typically unique to a family and are associated with reproductive risk. Here we report a rare case of a recurrent t(3;8)(p14.2;q24.1) translocation associated with increased risk of developing Renal Cell Carcinoma (RCC). The identification of such rearrangements by karyotyping enables cancer monitoring and potential early treatment intervention in addition to assessing reproductive risk for subsequent generations.

Introduction

In a constitutional setting balanced chromosomal rearrangements, such as reciprocal translocations, are widely recognized for their impact on reproductive outcomes. This may include sub-fertility, increased miscarriage risk, and the likelihood of producing offspring with unbalanced chromosomes that can cause developmental delay or congenital abnormalities. Whilst these reproductive consequence are well-documented, rarely these rearrangements are also associated with increased cancer risk.

Renal cell carcinoma (RCC) is the most common type of kidney cancer, originating in the lining of the renal tubules. Patients diagnosed with stage I and II cancer have a five-year survival rate ranging from 80% to 90%. Although the vast majority of cases arise sporadically, around 3% are familial, wherein inheritance of a chromosomal rearrangement infers cancer risk.[1]

One of these known familial rearrangements involves a translocation between the short arm of chromosome 3 and the long arm of chromosome 8 known as t(3;8)(p14.2;q24.1). Members of a family who inherit this translocation have an 80% cumulative probability of developing RCC by the age of 60. Typically, with a younger age of cancer onset than in sporadic RCC cases. This predisposition is likely due to disruption of tumour suppressor genes at the translocation breakpoints or loss of a derivative chromosome in renal cells.[1,2]

Identification of translocation carriers by karyotyping enables cancer monitoring and potential early treatment intervention, in addition to assessing reproductive risk for subsequent generations.

Case Study

The index case was a 37-year-old female referred for cytogenetic investigations due to a family history of RCC. The family pedigree showed that both the father and brother had been diagnosed with RCC. They were also known to carry a translocation involving chromosomes 3 and 8 (figure 1).

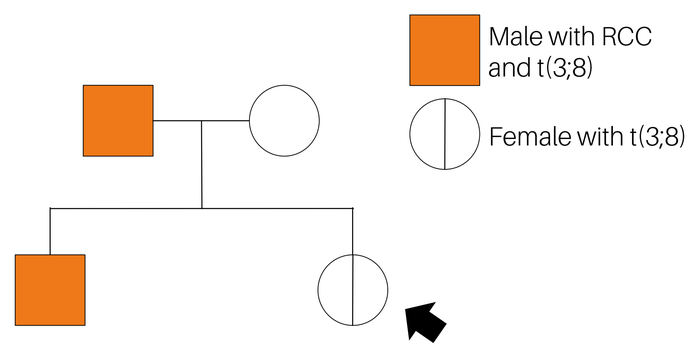

Figure 1. Family pedigree showing affected father and son with RCC and the index case who carries the translocation but has not yet manifested disease.

G band karyotyping of stimulated T-lymphocytes was performed using standard techniques. Results confirmed that the patient had inherited the t(3;8) translocation from her father (figure 2). Therefore, she is at risk of developing RCC in the future.

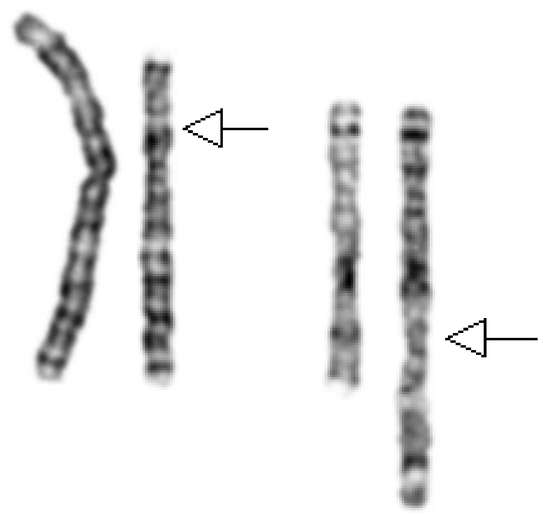

Figure 2: G-banded chromosomes show the reciprocal translocation involving exchange between the short arm of chromosome 3 and the long arm of chromosome 8 at breakpoint p13 and q24.1 respectively. p13 analogous to p14.2 but was reported for consistency with the historic reports.

Predicted reproductive outcomes for carriers of this translocation include progeny with a normal karyotype, balanced carrier status (with RCC risk) and unbalanced derivatives likely to result in implantation failure and/or early pregnancy loss (figure 3). The patient is at increased risk of recurrent miscarriages and for viable progeny who carry the t(3;8) there is a similar RCC risk.

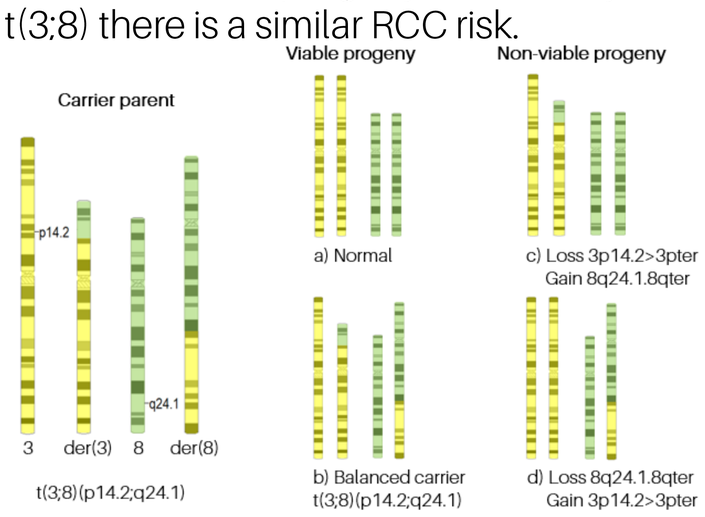

Figure 3: Meiosis segregation outcomes for carriers of t(3;8), for simplification only those outcomes with greatest potential for viability are shown.

An audit of our laboratory database from 2014-2024 identified one other case with the t(3;8) translocation segregating with RCC in a different family, highlighting that this translocation is a rare but recurrent finding in familial RCC cases.

Discussion/Conclusion

Here we present a rare case of a constitutional rearrangement inferring increased risk for RCC, segregating within a family. This case highlights the importance of cytogenetics in identifying carriers who are at increased risk of cancer, enabling monitoring and early treatment intervention, in addition to assessing the reproductive risk for the family. In the future, further research into the oncogenic mechanism of the t(3;8) will enable the refinement of screening protocols, early intervention and the development of targeted therapies.

Reference

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2. Glover T W, Coyle-Morris J F, Li F P, Brown R S, Berger C S, Gemmil R M, Hecht F. Translocation t(3,8)(p14.2;p24.1) in Renal Cell Carcinoma Affects Expression of the common Fragile Site at 3p14 (FRA3B) in Lymphocytes. *Cancer Genet Cytogenet. 1988 Mar;31(1):69-73*